

Enhancement of osteogenesis by polyphosphoesters having bone affinity

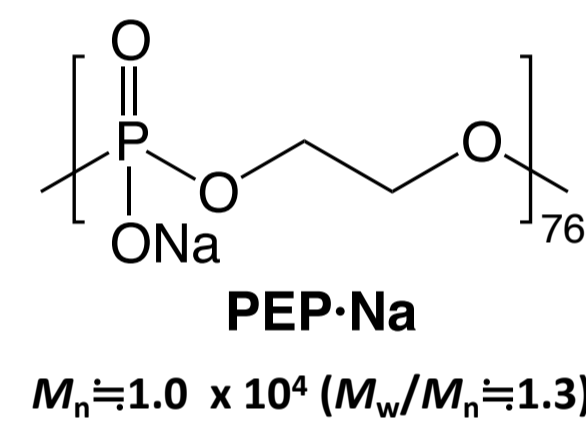
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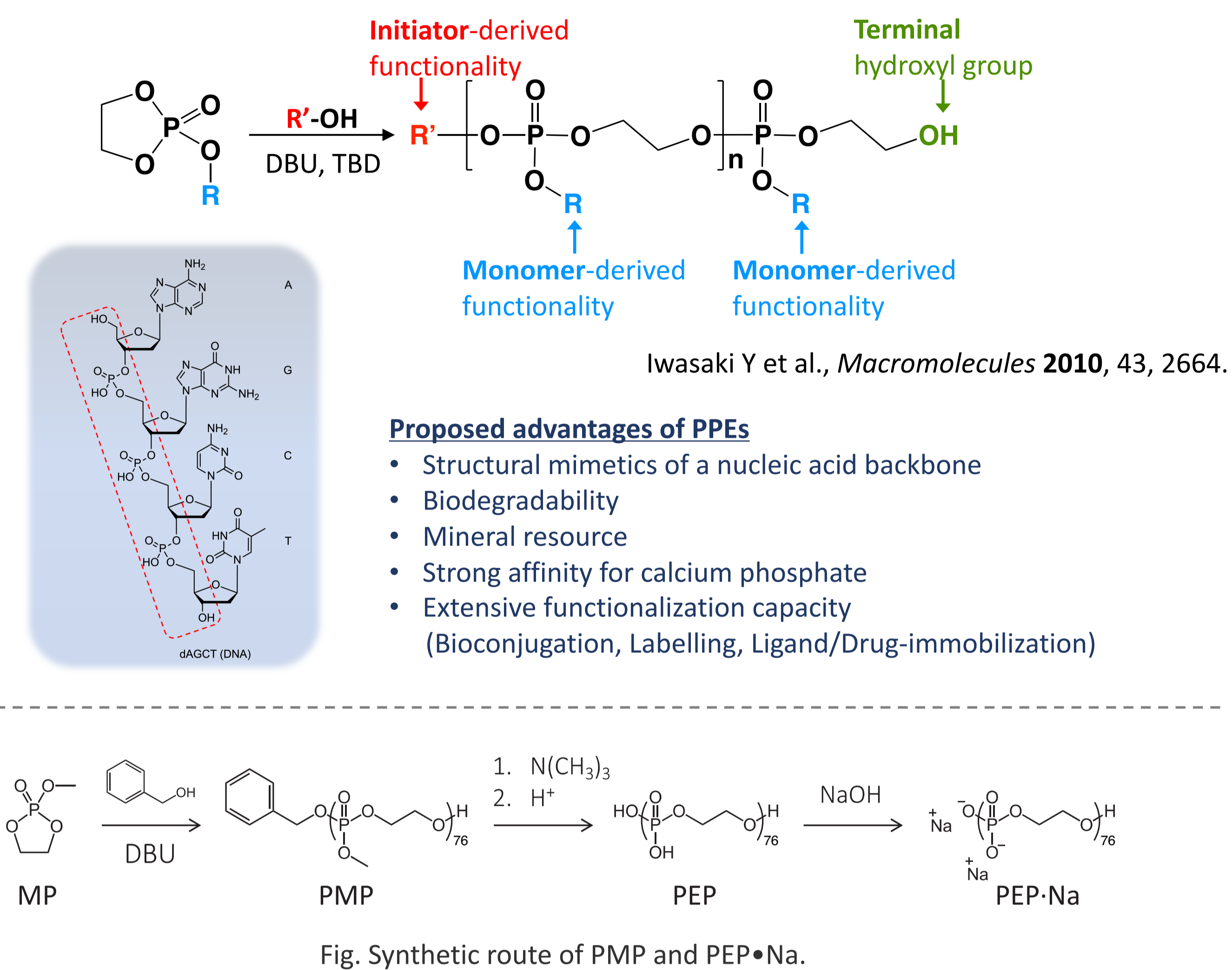
Introduction

Bone diseases such as osteoporosis and osteolysis involving hyperactivity in osteoclasts have significant physical, emotional, and financial consequences. Many potential drugs are effective in treating diseases but result in side effects preventing their efficacy in the clinic.

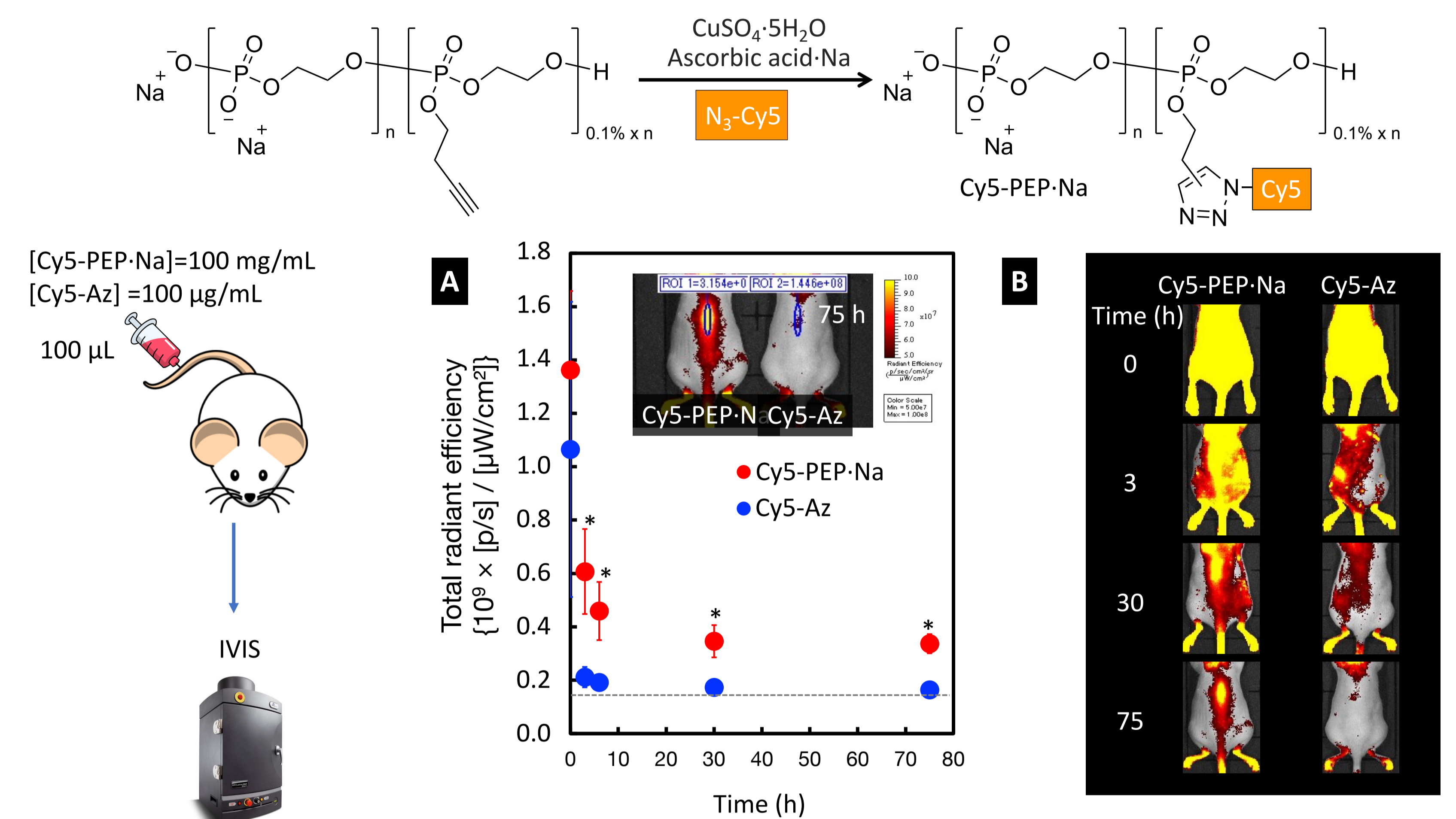
The motivation of this study is to emerge polymer therapeutics for bone treatment. The viability and function of human osteoclasts and murine osteoblast precursors in contact with poly(ethylene sodium phosphate) (PEP·Na) were investigated. Moreover, we determined the biodistribution of PEP·Na after intravascular injection to understand the bone affinity of PEP·Na.



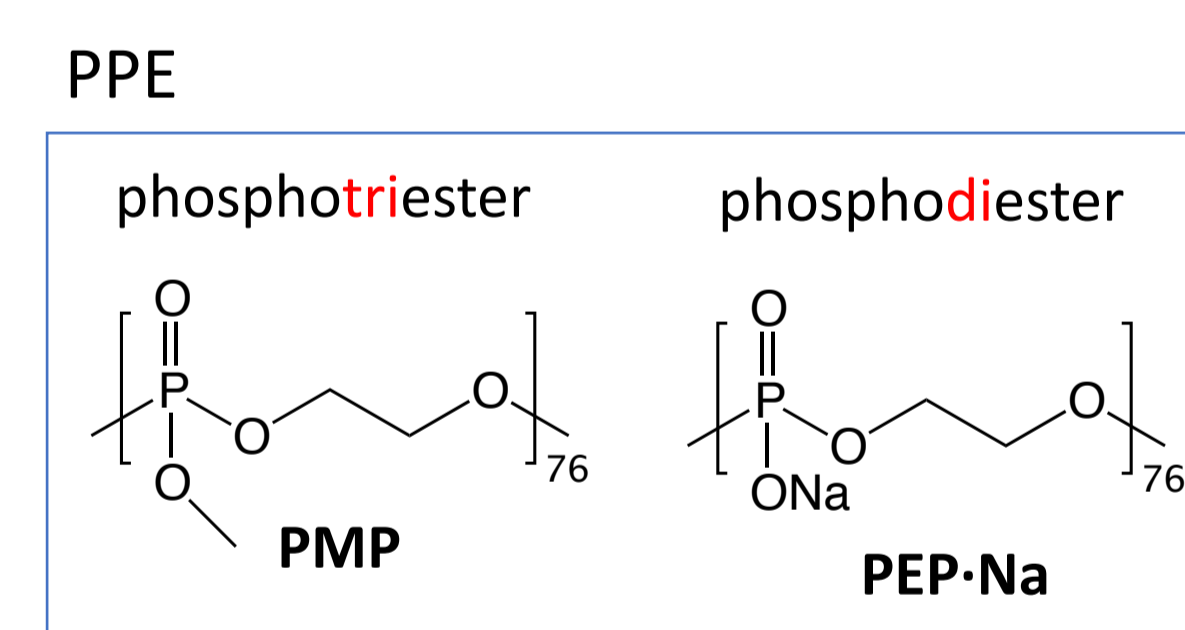
Polyphosphoester (PPE)



Bone Affinity



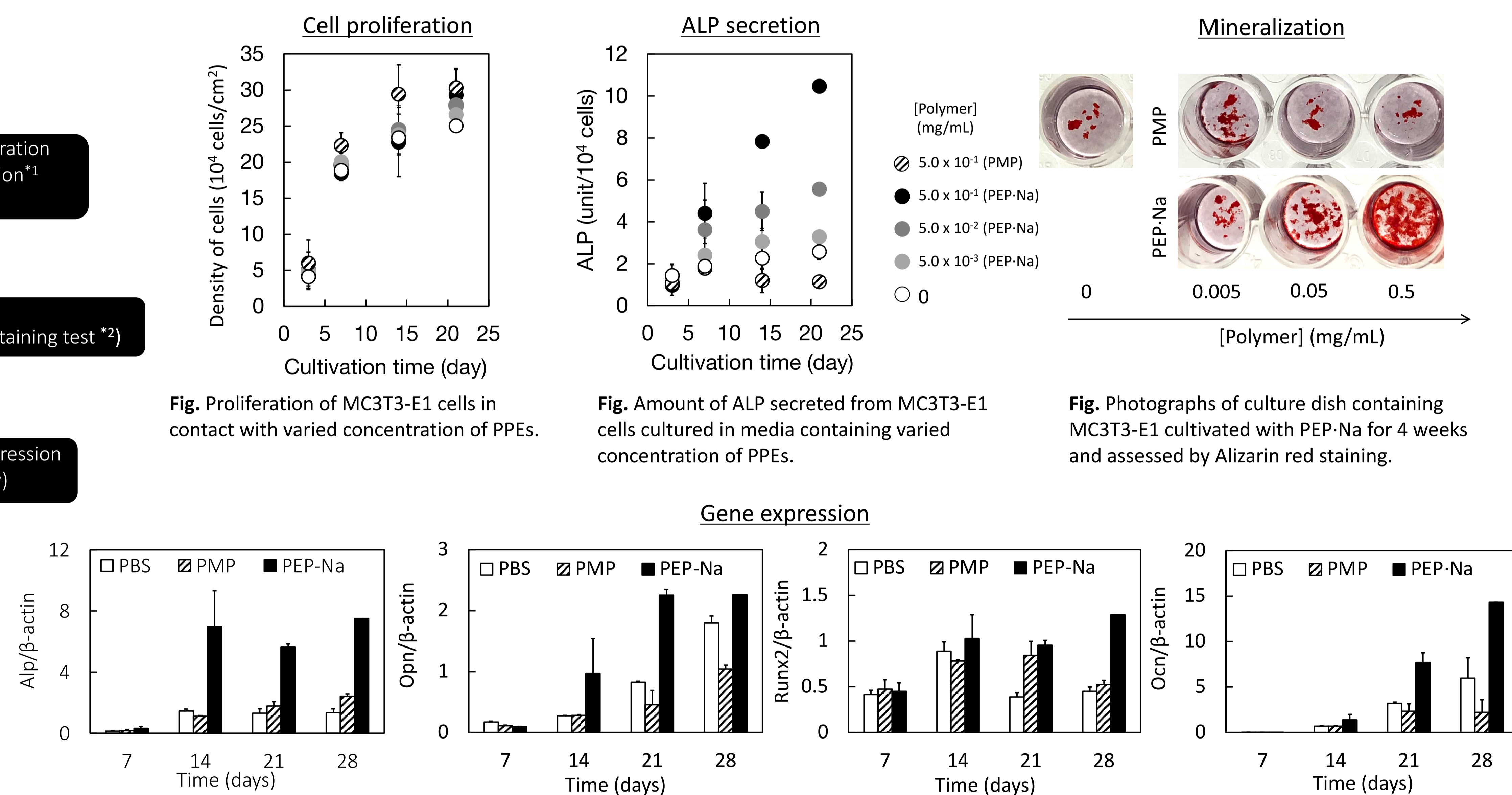
Osteoblastic function



Culture dish → PMP or PEP·Na → Culture dish

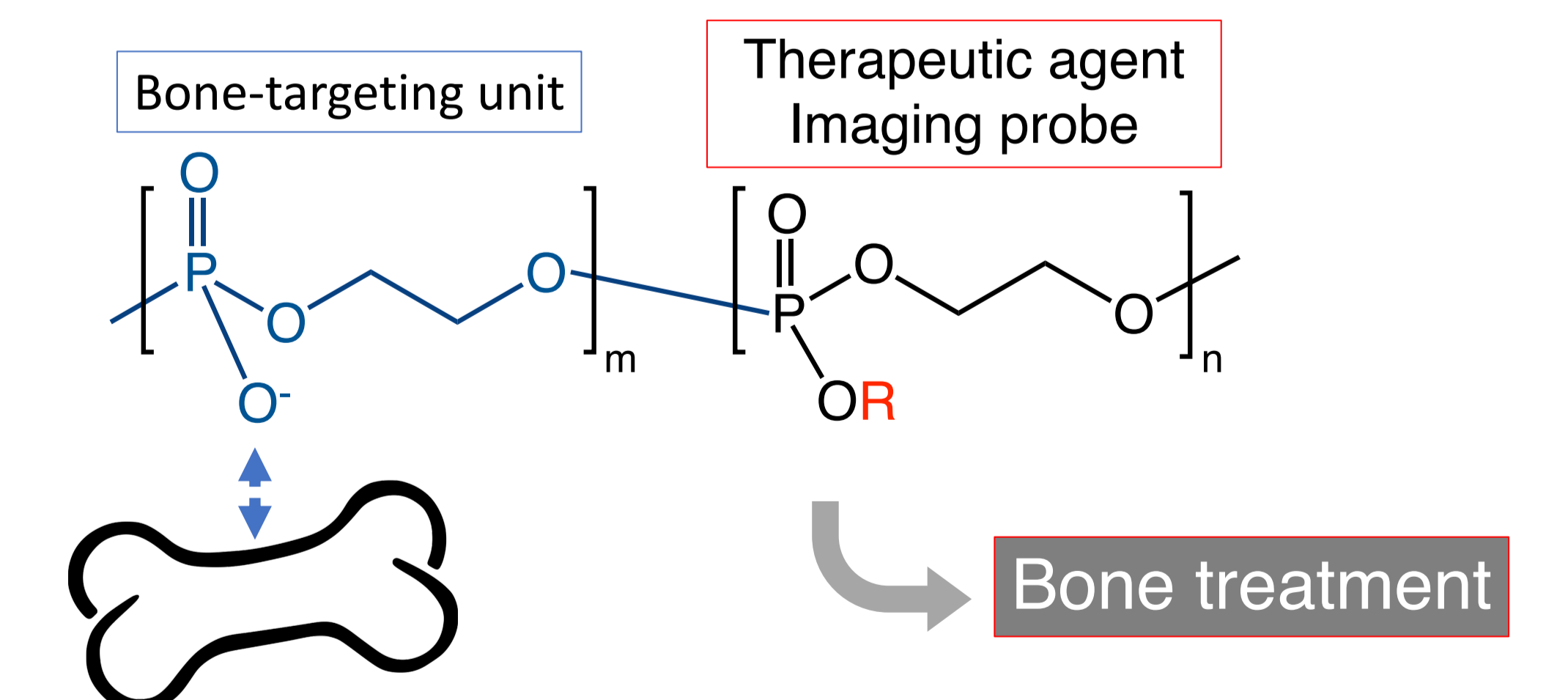
MEM- α + 10%FBS
[Glycerophosphate disodium salt] = 10 mM
[Ascorbic acid] = 50 μ g/mL

*¹ ALP: Alkaline phosphatase, a reliable marker of osteoblast differentiation
*² Alizarin-Red staining is used to detect calcium deposits generated from differentiated osteoblasts.
*³ RT-PCR: Determination of Osteoblastic gene markers



Conclusion

In the present study, we evaluated the effects of PEP·Na on bone cell viability and activity. PEP·Na exhibited excellent short-term biocompatibility with osteoblasts. In contrast, selective inhibition of osteoclast adhesion and function was observed following cultivation with PEP·Na. Moreover, we have demonstrated that PEP·Na shows good affinity for bone *in vivo*. Due to the molecular diversity of polyphosphoesters, various types of polymeric prodrugs for bone disease treatment can be designed based on PEP·Na.



Acknowledgements



References

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- Iwasaki Y et al., Bone-targeting poly(ethylene sodium phosphate), *Biomater. Sci.* **2018**;6:91-95.
- Hirano Y et al., Bone-specific poly(ethylene sodium phosphate)-bearing biodegradable nanoparticles, *Colloids Surf., B* **2017**;153:104-110.